MA ~~51217~~ 51265 8EHQ-0901-14880

DuPont Haskell Laboratory
for Health and Environmental Sciences
Elkton Road, P.O. Box 50
Newark, DE 19714-0050

August 31, 2001

2001 SEP -4

Via Federal Express

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Attention: 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
401 M Street SW
Washington, D.C. 20460-0001

Contain NO CBI

Dear 8(e) Coordinator:

8EHQ-01-14880
Alcohols, C8-14, γ-ω-perfluoro
[CAS # 68391-08-2]

This letter is to inform you of the results of a recently completed 90-day oral gavage study with a one-generation reproduction study in rats with the above referenced test material. Based on the certificate of analysis, the test material contains approximately two (2) weight-percent CAS # 68188-12-5, Alkyl iodides, C4-20, γ-ω-perfluoro.

The test material was administered by gavage to 4 groups of male and female rats at dosages of 0, 25, 100, or 250 mg/kg/day for approximately 90 days. In the subchronic study, body weights, food consumption, and clinical signs were evaluated weekly. Clinical pathology endpoints were evaluated on weeks 7 and 13 of the study, and following a 36- and 92-day recovery period. The rate of hepatic β-oxidation, a measure of peroxisome proliferation, was determined in rats following approximately 10 or 90 days of treatment and after a 36- and 92-day recovery period. Neurobehavioral and ophthalmology assessments were also performed prior to dosing, during week 13, and near the end of the 36-day recovery period. After approximately 90 days of dosing, 10 rats/sex/dose level were sacrificed and given a gross and microscopic pathology examination. After 36 days of recovery, 10 rats/sex from the control and high dose group were evaluated and an additional 5/sex/dose were evaluated at the 92-day recovery period.

After approximately 70 days of dosing, subgroups of 20 rats/sex/dose continued to be dosed and were bred, allowed to deliver litters, and maintained until sacrifice after siring litters (males) or weaning of litters on lactation day 21 (females). Selected pups were sacrificed on post-natal day (PND) 21 for pathological evaluation. One pup/sex/litter was monitored up to approximately PND 30 for developmental landmarks.

There were a number of significant findings in the 90-day subchronic study. Body weights and/or nutritional parameters were statistically significantly reduced in male and female rats dosed at 100 and 250 mg/kg/day. These parameters were comparable to the respective controls after either the 36-day or 92-day recovery periods.

There was a statistically significant increase in the number of clinically observed broken (males) and absent teeth (males and females) in the 250 mg/kg/day dose group. Compound-related microscopic tooth lesions were observed in the 100 and 250 mg/kg/day male and female subchronic rats. These tooth lesions consisted of degeneration and/or disorganization of enamel organ ameloblast cells. Ameloblast degeneration/disorganization was still present in male and female 36-day recovery rats at 250 mg/kg/day and in males (100 and 250 mg/kg/day) and females (250 mg/kg/day) at the end of the 92-day recovery period.

Males and females dosed with 250 mg/kg/day had decreased red cell mass parameters, along with correlative changes in other hematology parameters and in red cell morphology. After a 36-day recovery, mean red cell mass of female rats was similar to the control group, although some changes were still present in other hematologic parameters. However, male rats still had decreased red cell mass effects, and associated alterations in other hematologic parameters. Additionally, at termination of dosing, compound-related but non-adverse changes occurred in coagulation, clinical chemistry, and urinalysis parameters. Plasma fluoride was elevated in males and females dosed with 100 and 250 mg/kg/day. Urine fluoride was elevated in males and females dosed with 25, 100, or 250 mg/kg/day.

Statistically significant increases, compared to controls, in mean liver weights occurred in the 100 and 250 mg/kg/day male and female groups after approximately 90 days of dosing. After the recovery periods, liver weights were still increased in the 250 mg/kg/day male (36- and 92-day) and female (92-day only) groups. The increased liver weights in males correlated with microscopic hepatocellular hypertrophy. Increased liver weight in females correlated with hepatocellular hypertrophy only in the 250 mg/kg/day subchronic toxicity group. A dose-dependent increase in the rate of hepatic β-oxidation also occurred following 10 or 90 days of dosing, with statistical significance observed in the 100 and 250 mg/kg/day male and female groups. Following the recovery periods, statistically significant increases in rate were observed only in the 250 mg/kg/day male and females.

Statistically significant elevations in mean kidney weights occurred in the 100 and 250 mg/kg/day male and 25, 100, and 250 mg/kg/day female rats at 90 days. After the recovery periods, kidney weights were still increased in the 250 mg/kg/day male and female (92-day only) groups. Elevated kidney weights in males correlated with microscopic tubular hypertrophy in the 100 and 250 mg/kg/day subchronic toxicity males and 250 mg/kg/day 36-day recovery males. There were no microscopic correlates in females.

Follicular hypertrophy was present in thyroid glands of the 100 and 250 mg/kg/day male and 250 mg/kg/day female rats at 90 days. Hypertrophy was not present in the 25 mg/kg/day groups at 90 days nor in the recovery groups at any dose level.

Several significant effects were also observed in the reproduction evaluations. At 250 mg/kg/day, there were statistically significant reductions (% of control) in the number of pups born (85%), the number of pups born alive (83%) and the number of pups alive on day 4 of lactation (81%). Implantation efficiency was significantly reduced (84.5% compared to 96.6% in the control group), which reflects the reduction in the number of pups born. There were no significant reductions in pup survival during lactation. Pup weights were also significantly reduced.

At 100 mg/kg/day, there were compound-related reductions (magnitude similar to the 250 mg/kg/day group) in the number of pups born and born alive. In addition, there was a significant reduction in the number of pups alive at day 4 (68% of control). There were no significant reductions in pup survival during lactation. A significant reduction in implantation efficiency (magnitude similar to 250 mg/kg/day group) occurred at 100 mg/kg/day.

At 25 mg/kg/day, there were no effects on the number of pups, pup viability, survival or pup weights.

At 100 and 250 mg/kg/day, there was a statistically significant increase in testicular spermatid numbers (20 and 10% greater than control, respectively) in P_1 male rats. This finding was not considered compound-related since the means for these groups were within the historical control range for previous studies and the increase appeared to be due to a slightly lower than usual mean in the control group. In addition, there were no testicular weight effects nor corroborative histopathology effects.

Under these experimental conditions, the findings described above appear to be reportable, based upon guidance given in the EPA TSCA Section 8(e) Reporting Guide (June 1991).

Sincerely,

Robert W Rickard for AMK

A. Michael Kaplan, Ph.D.
Director – Regulatory Affairs

AMK/GSL:clp
(302) 366-5260

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